(c) The recited time course of blood serum concentration is now one wherein a blood serum concentration of 20 ng/ml (a threshold concentration for therapeutic effect), reached within about 0.5 h, is an essential feature. In Claim 1 as originally filed, the corresponding feature (condition (a)) was not essential, so long as at least one of conditions (b) and (c) were met. Support for a blood serum concentration of 20 ng/ml reached within about 0.5 h is found in the specification at least at page 5 lines 6–7.

(d) The amount of valdecoxib per dose of the composition is now given as about 5 mg to about 40 mg (*i.e.*, incorporating the essential feature of original Claim 4, now cancelled).

Claim 3 is amended as to dependency and to remove redundancies arising from amendment herein of Claim 1.

No new matter is introduced and no change in inventorship results from the amendments proposed herein.

RESPONSE TO OFFICE ACTION DATED DECEMBER 31, 2001

Claims 1–18 stand rejected in the above-referenced application. Claims 2 and 4 are cancelled by the present amendment. Claims 1, 3 and 5–18 are pending in the application.

All pending claims stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gao *et al.* (WO 00/32189) in view of Lai *et al.* (US 6,306,842) and Delgado *et al.* (US 6,323,226). This rejection is respectfully traversed.

It is noted that the filing date of Lai is June 2, 2000, later than the filing date of each of the three applications from which the present application draws priority. It is further noted that both Lai and Delgado issued as U.S. Patents after the filing date of the present application. No statement herein is to be construed as an admission that either Lai or Delgado is prior art to the present invention under 35 U.S.C. § 102(e) or otherwise.

1. The Gao reference is not available as prior art under 35 U.S.C. § 103(c)

WO 00/32189 (Gao) published June 8, 2000, after the filing date of each of the three applications from which the present application claims priority. Therefore, Gao is not available as prior art under 35 U.S.C. § 102(a) or (b). To the extent that Gao could be prior art under 35 U.S.C. § 102(e), Examiner's attention is respectfully drawn to the fact that the present

application and Gao were, at the time Applicant's present invention was made, subject to an obligation of assignment to the same entity. Therefore, under 35 U.S.C. § 103(c), Gao is not available as prior art in the present rejection.

However, Examiner's attention is respectfully drawn to an earlier publication related to the Gao reference, namely Ecuador Patent Application No. 98-2761 (hereinafter "EC 98-2761"), believed by Applicant to have been laid open on May 6, 1999, an English language copy of which is provided herewith. For Examiner's convenience, an additional copy of EC 98-2761 in its English language version is provided as part of a Supplemental Information Disclosure Statement which is submitted under separate cover.

It is noted that EC 98-2761 is not prior art under 35 U.S.C. § 102(b), having been published less than one year before the earliest priority date of the present application (December 9, 1999). Even if EC 98-2761 were prior art under 35 U.S.C. § 102(a), which is not admitted herein, the present invention would not have been obvious over EC 98-2761 in view of Lai and Delgado, as more fully explained below.

2. No *prima facie* case of obviousness has been made

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the references when combined must teach or suggest all the claim limitations. See MPEP § 2143.

As shown below, no such *prima facie* case of obviousness can be made against the present claims.

There was no reasonable expectation of success at the time the invention was made.

Even if a person of ordinary skill in the art would have been motivated to modify or combine EC 98-2761 with either or both of Lai and Delgado, which is not admitted herein, such a person would not have done so with a reasonable expectation of success.

EC 98-2761 teaches that celecoxib is preferably formulated in a dosage amount of about 50 mg to about 800 mg, more preferably about 75 mg to about 400 mg, and still more preferably about 100 mg to about 200 mg (EC 98-2761, page 14 lines 22–24). The present valdecoxib

compositions are formulated in a much lower dosage amount, about 5 mg to about 40 mg as recited in Claim 1 as amended herein.

Furthermore, EC 98-2761 discloses celecoxib pharmacokinetic studies in adult human subjects wherein the amount of celecoxib administered was 300 mg (Example 13, see page 58 lines 15–17), 200 mg (Example 16, see page 62 lines 2–5), 50 mg and 100 mg (Example 17, see page 64 lines 7–11), or 200 mg (Example 18, see page 67 lines 5–8). By contrast, as little as 20 mg valdecoxib in a composition of the present invention is disclosed in the present specification to provide a therapeutically effective concentration in blood serum within about 0.5 h after oral administration.

Thus, although celecoxib and valdecoxib have similar modes of action and therapeutic utility, they are very different drugs pharmacologically, at least with respect to dose range. By simply listing celecoxib and valdecoxib as illustrative selective COX-2 inhibitory drugs, neither Lai nor Delgado motivates the ordinary skilled artisan reading EC 98-2761 to consider formulating valdecoxib in place of celecoxib in such markedly different dosage amounts, nor gives rise to a reasonable expectation of success in doing so. The ordinary skilled artisan reading Lai and Delgado would be led to consider celecoxib and valdecoxib to be substantially interchangeable, which it is clear from a comparison of EC 98-2761 with the present application they are not.

Thus the teaching of EC 98-2761 in view of Lai and Delgado indicates no reasonable expectation of success and thereby defeats one of the necessary criteria for establishing a *prima facie* case of obviousness (MPEP § 2143).

The cited art fails to disclose every limitation of the present claims.

Examiner correctly notes that Gao is silent as to valdecoxib. Lai and Delgado each mention valdecoxib, but without any indication of dose range. Thus at least one limitation of the present claims as amended herein, namely a valdecoxib dosage amount of about 5 mg to about 40 mg, is missing from the cited art.

Thus no reading of Gao in view of Lai and/or Delgado discloses every limitation of the present claims. The cited art therefore lacks one of the necessary criteria for establishing a *prima facie* case of obviousness (MPEP § 2143).

Conclusion: no *prima facie* case for obviousness can be made against the present claims.

Because at least the second and third prongs of the test for *prima facie* obviousness as set out in MPEP § 2143 have not been met, no *prima facie* case for obviousness can be made. Withdrawal of the rejection under 35 U.S.C. § 103(a) as unpatentable over Gao (as represented by EC 98-2761) in view of Lai and Delgado is therefore respectfully requested.

The present application, following amendment as proposed herein, is believed to be in condition for allowance.

Respectfully submitted,

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Enclosures:
Amendments in marked-up form in accordance with 37 C.F.R. § 1.121(c)(1)(ii)
Copy of EC 98-2761 in English language version

MARKED UP VERSION OF AMENDMENTS MADE IN CLAIMS

1. (Amended) A pharmaceutical composition comprising particulate valdecoxib in an amount of about [1] 5 mg to about [100] 40 mg per dose and one or more pharmaceutically acceptable excipients, wherein a single [dose, upon] oral administration of the composition, in an amount containing about 20 mg of valdecoxib, to a fasting subject[,] provides a time course of blood serum concentration of valdecoxib having [at least one of (a)] a time to reach a [threshold] concentration [for therapeutic effect] of 20 ng/ml not greater than about 0.5 h after administration[; (b) a time to reach maximum concentration (T_{max}) not greater than about 5 h after administration; and (c) a maximum concentration (C_{max}) not less than about 100 ng/ml].

2. (Amended) The composition of Claim [2] 1 wherein [a single dose, upon oral administration to a fasting subject, provides a time course of blood serum concentration of valdecoxib having each of (a) a time to reach a concentration of 20 ng/ml not greater than about 0.5 h after administration; (b)] said time course of blood serum concentration of valdecoxib has a time to reach maximum concentration (T_{max}) not greater than about 3 h after administration[;] and [(c)] a maximum concentration (C_{max}) not less than about 100 ng/ml.